



# Assessment of the Quality of Life Impact of Medical Devices

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*Plymouth Meeting, PA ,November 4, 1999*

# Quality of Life

## Definitional Elements

- ▶ Prolonging Life
- ▶ Relieving Distress
- ▶ Restoring Function
- ▶ Preventing Disability

Lembke, 1952



# FDA and New Therapeutics

## Responsibilities

- ▶ Approve Initial Marketing efficacy Claims based on *Clinical Benefit*
  - Prevent
  - Cure
  - Ameliorate
  - Alter Body Function
- Note: change in test or lab result is not sufficient unless the lab result has well established clinical meaning

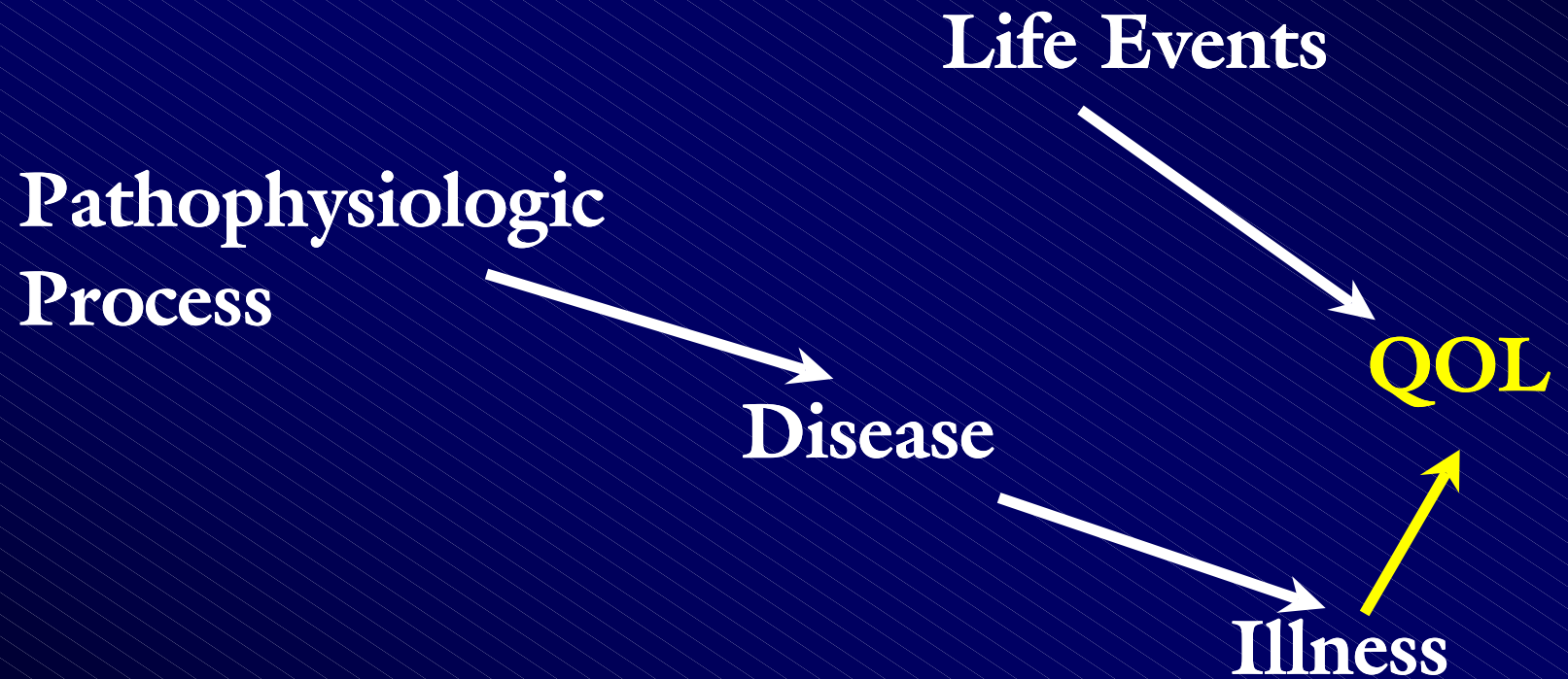
# Quality of Life Scales

## What do they measure?

- Improved Survival ?
  - Disease free survival
  - Quality adjusted survival
- Improved symptom profiles ?
  - Disease specific symptoms
  - Disability assessment
- Global perception of function ?

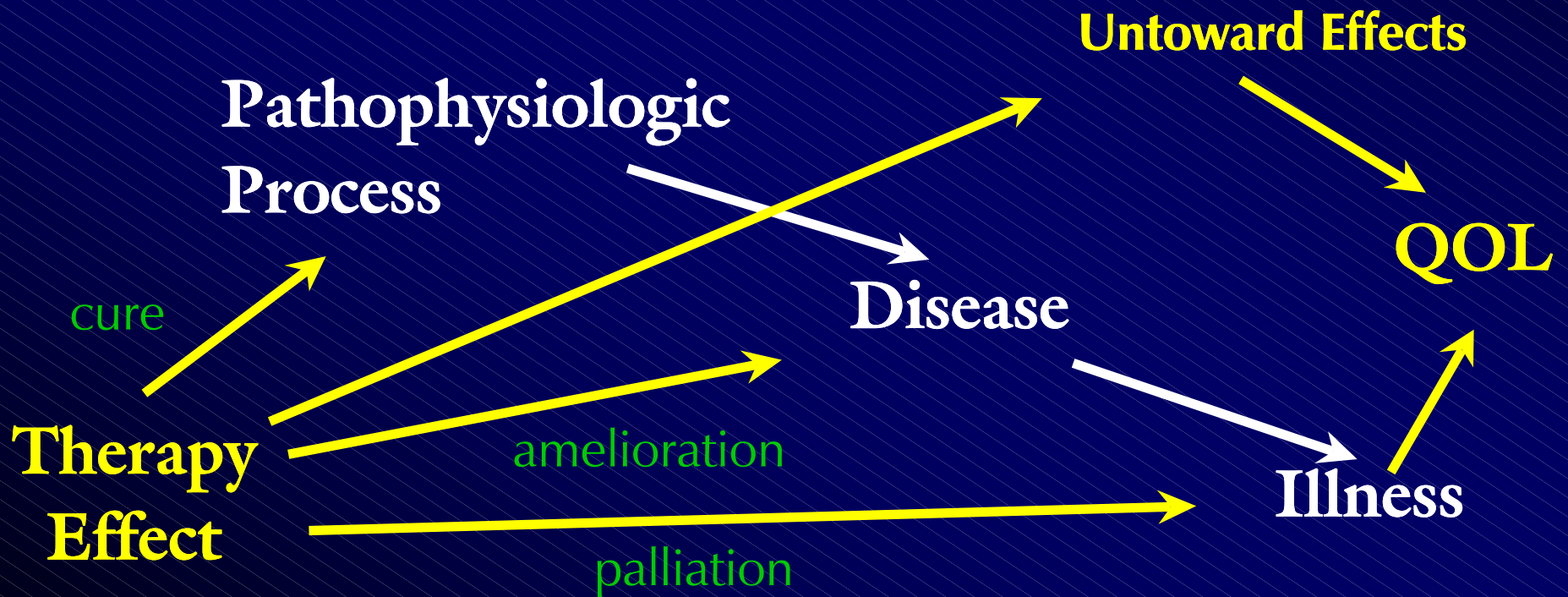
# Quality of Life

## Disease –Therapy Model



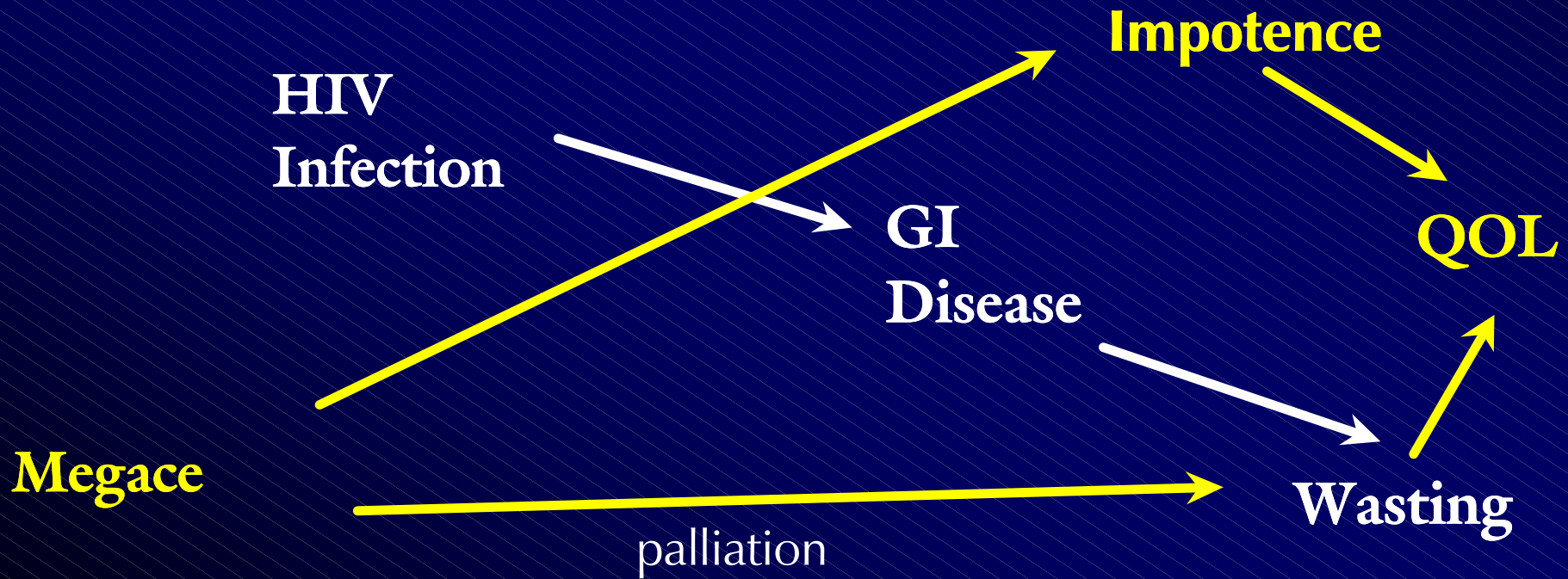
# Quality of Life

## Disease –Therapy Model



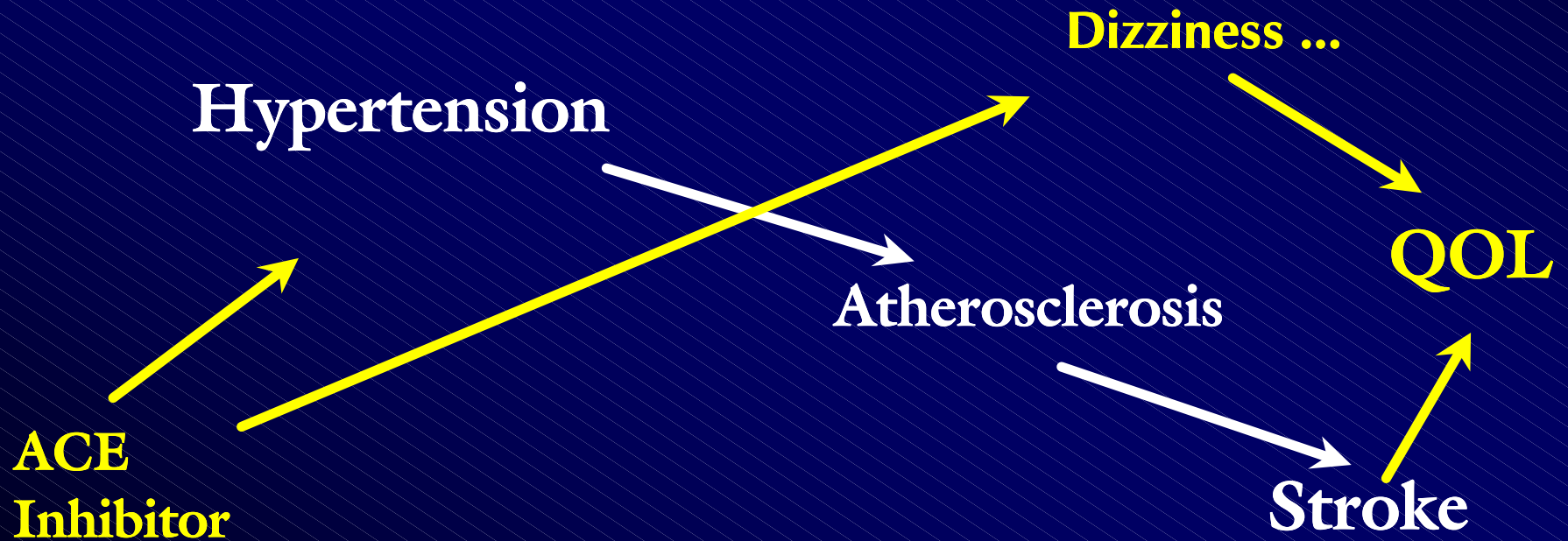
# Quality of Life

## Disease - Therapy Model



# Quality of Life

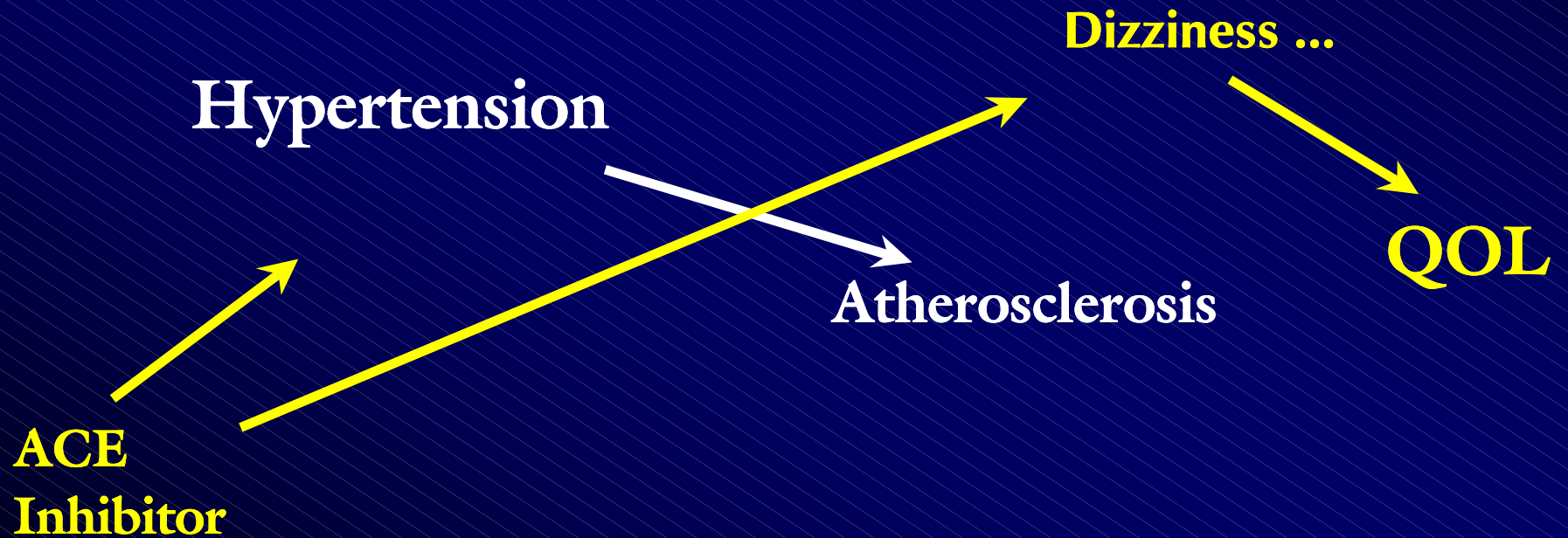
## Disease – Therapy Model





# Quality of Life

## Disease – Therapy Model



# Quality of Life: A Case Study

## New Antiviral vs. Continued AZT

- Randomized double blind study
- 500 participants followed 6 months
- Antiviral effects assessed by change in CD4 count, quantitative viral culture
- Quality of Life assessed with
  - Karnofsky Performance Status
  - MOS
  - Spitzer

# Quality of Life

## Karnofsky Scale

- 100 Asymptomatic, normal Function
- 80-90 Symptomatic, fully ambulatory
- 60-70 Symptomatic, in bed <50% of day
- 40-50 Symptomatic, in bed >50% of day
- 20-30 Bedridden
- 0 Death

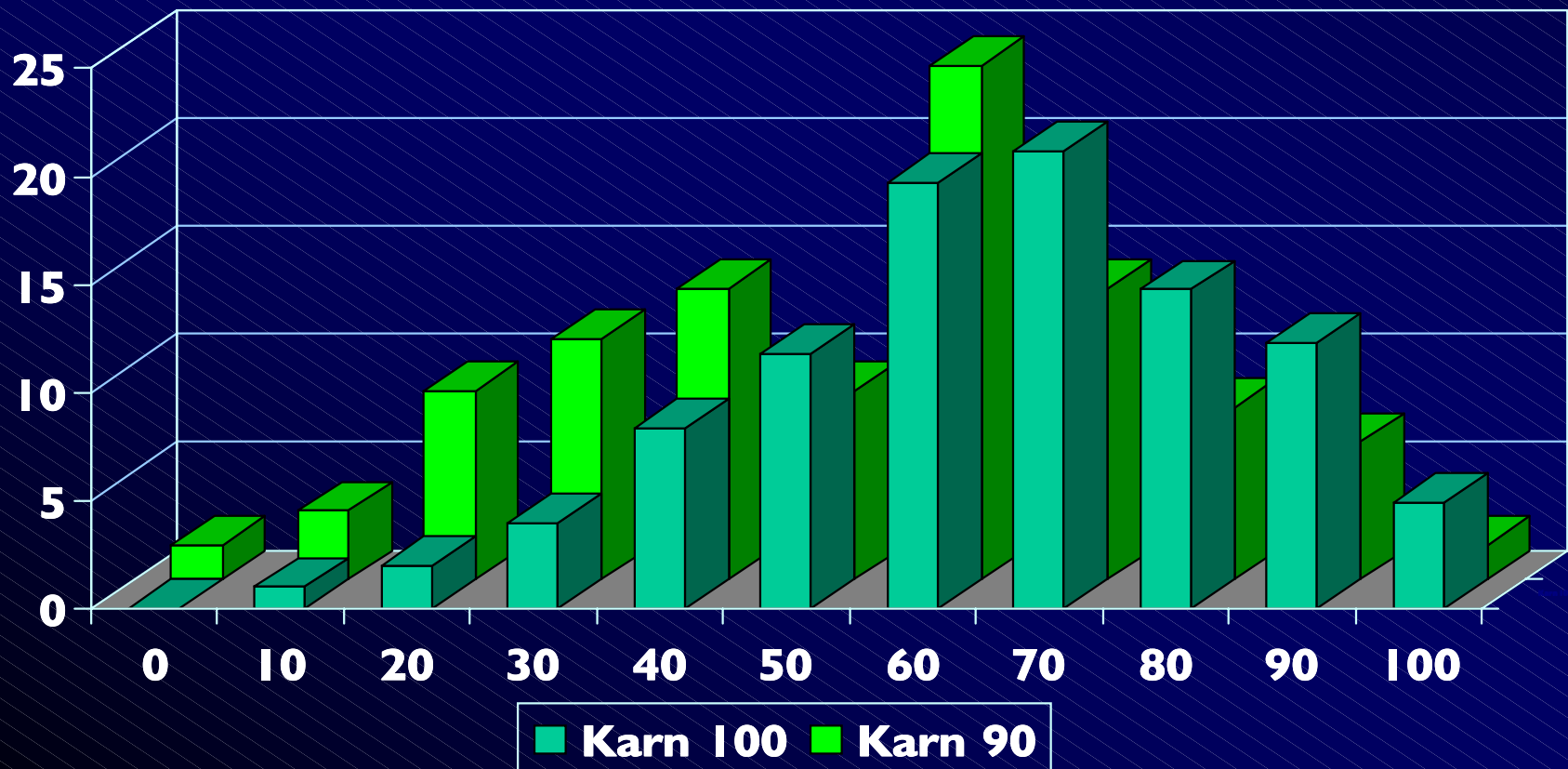
# Quality of Life

## MOS Framework of Health Indicators

- Clinical Status
- Physical functioning and well-being
- Mental functioning and well-being
- Social/role functioning and well-being
- General health perceptions and satisfaction

# Quality of Life Scales

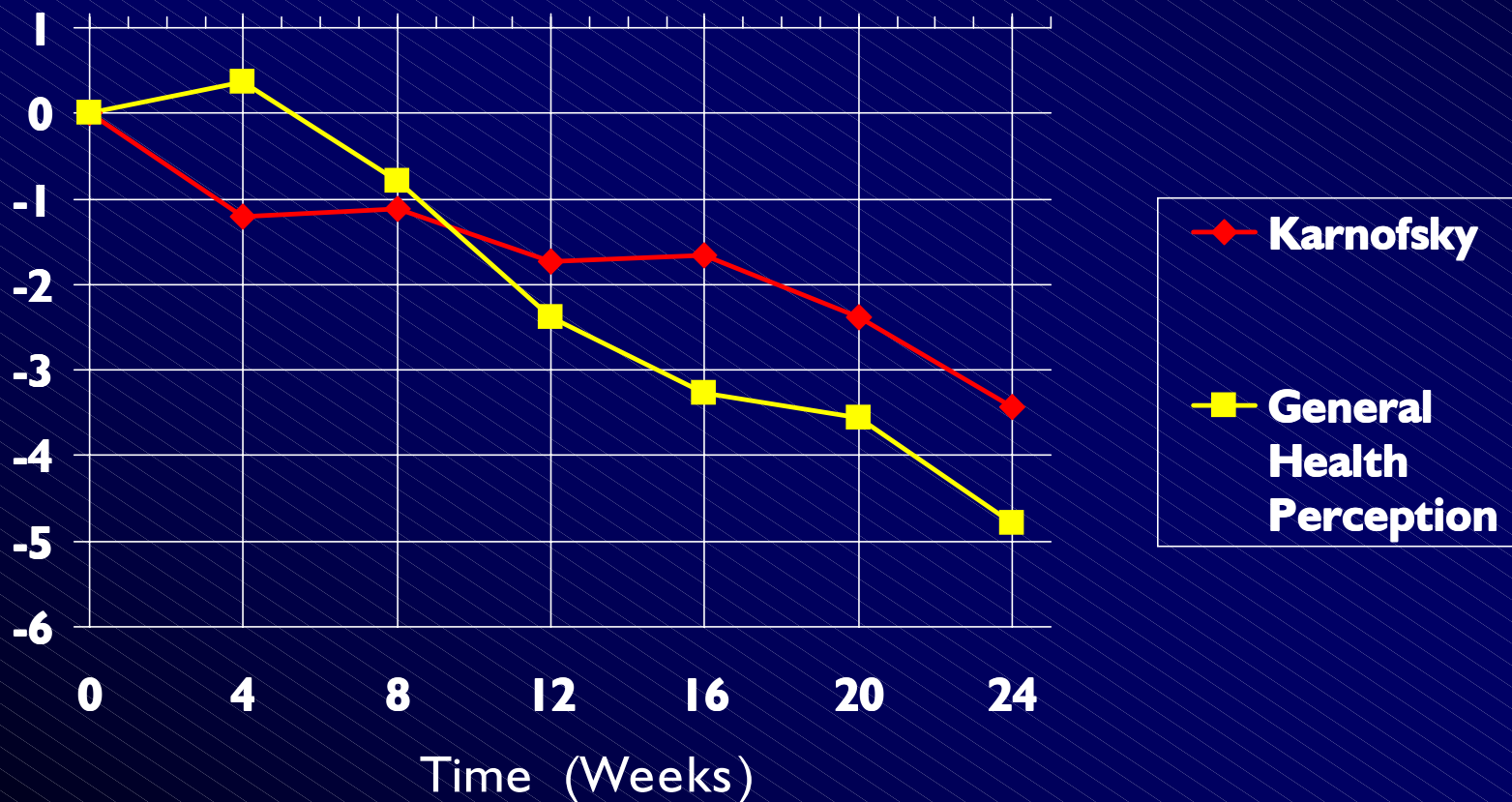
## General Health Perception Scale



# Quality of Life Scales

## Karnofsky and General Health Perception

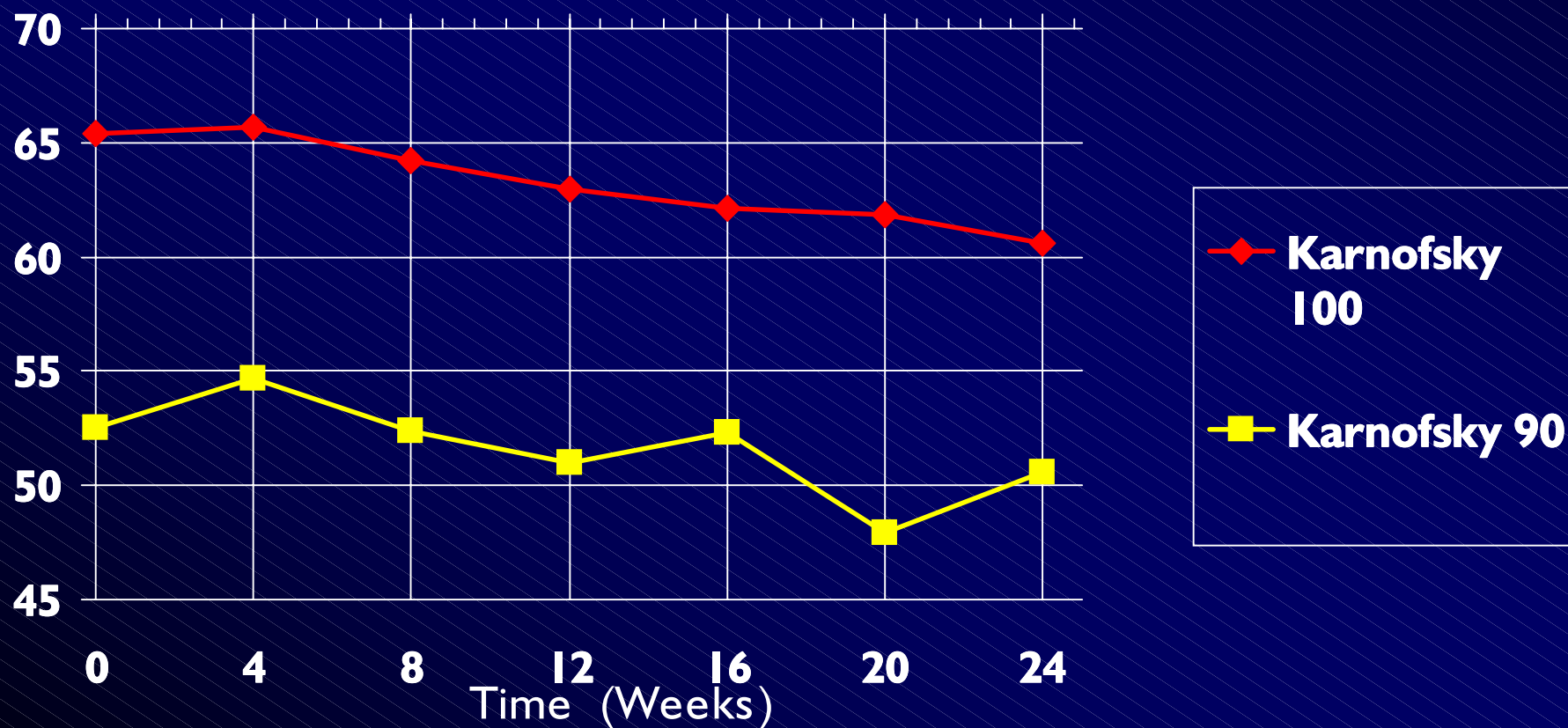
Change from Baseline in subgroup with Karnofsky = 100 at Baseline



# Quality of Life Scales

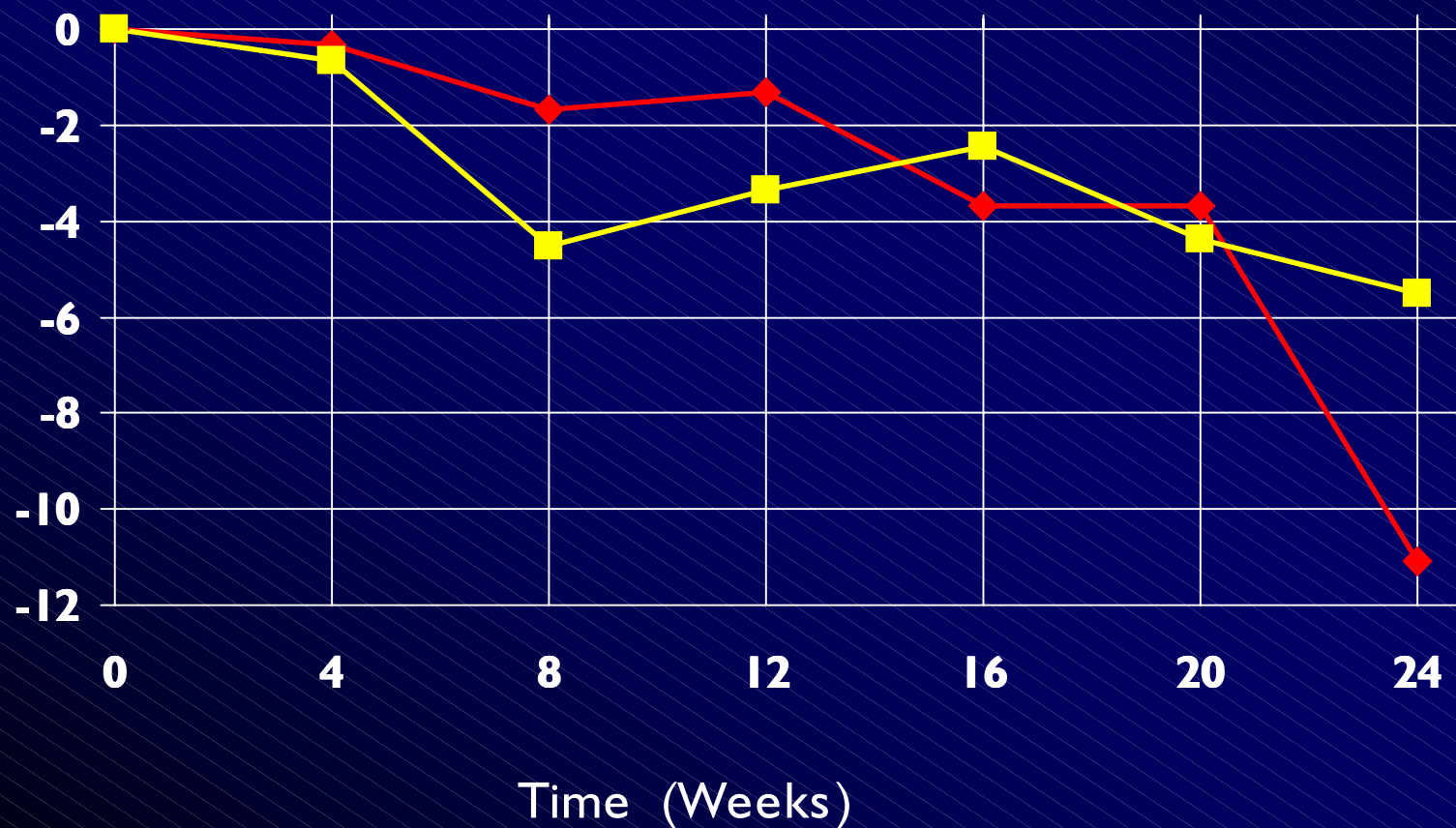
## General Health Perception

Change from Baseline Stratified by Karnofsky at Baseline



# Quality of Life Scales

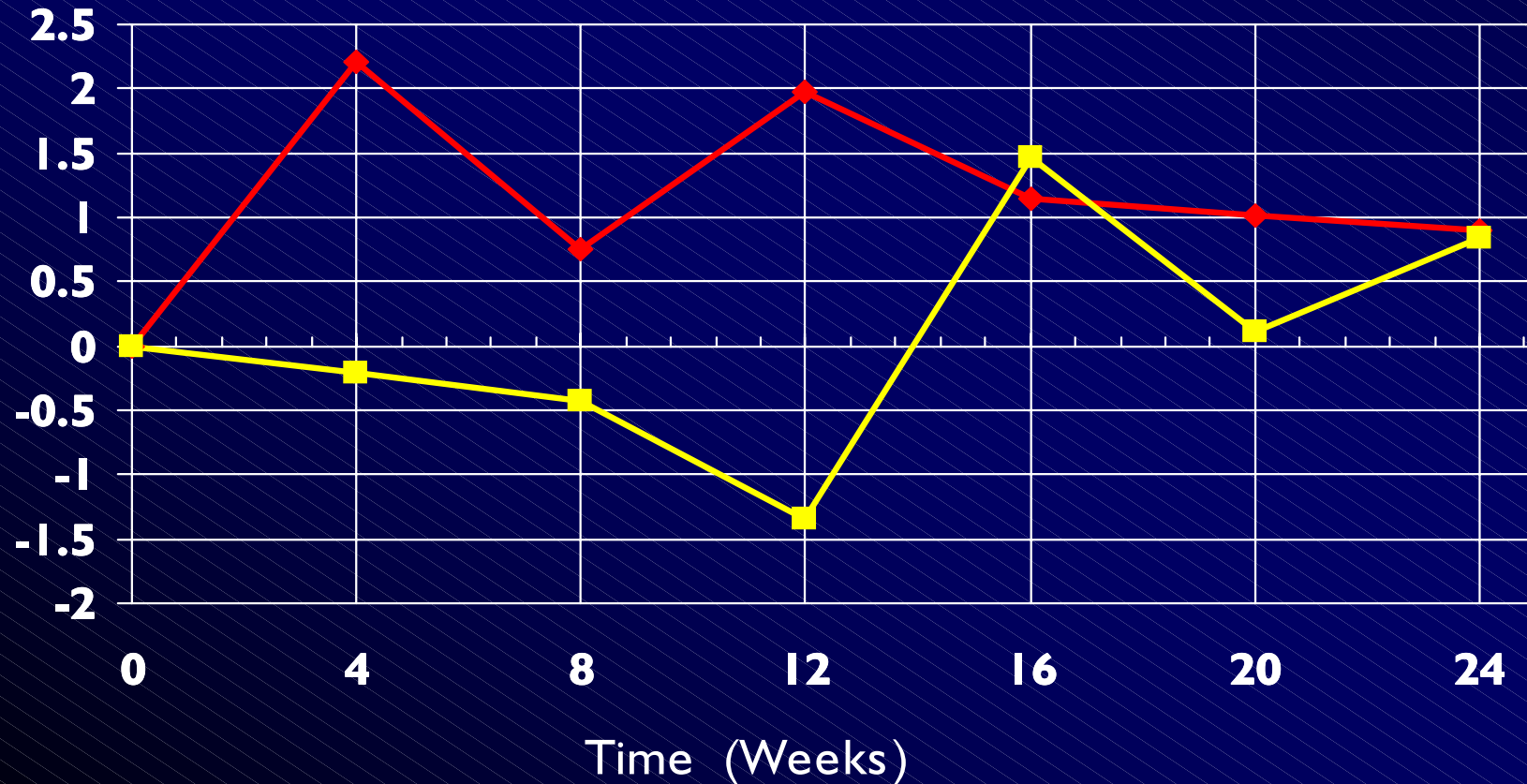
## Pain Scale: Change in baseline by Drug





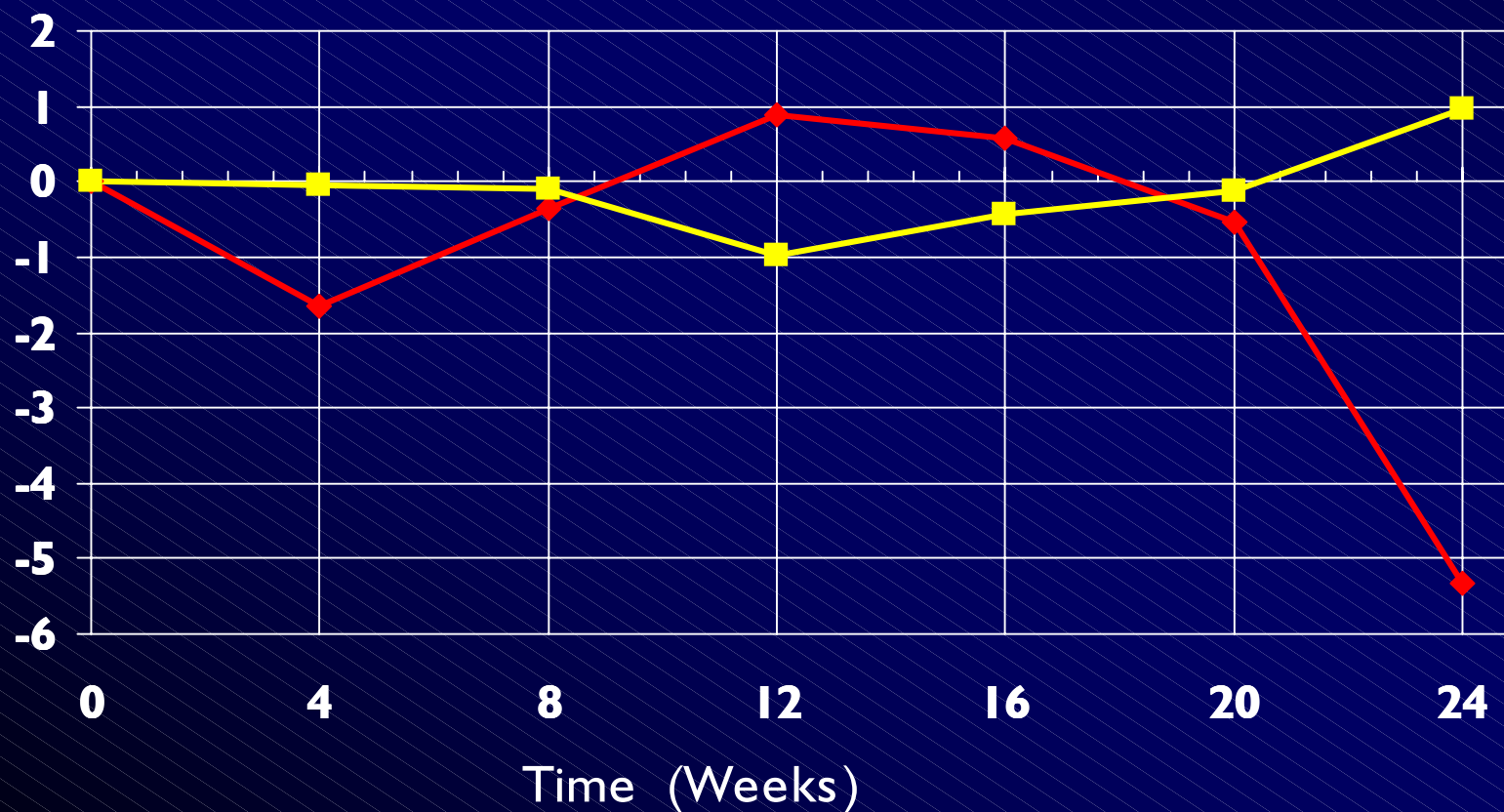
# Quality of Life Scales

## Mental Health Index: Change in baseline by Drug



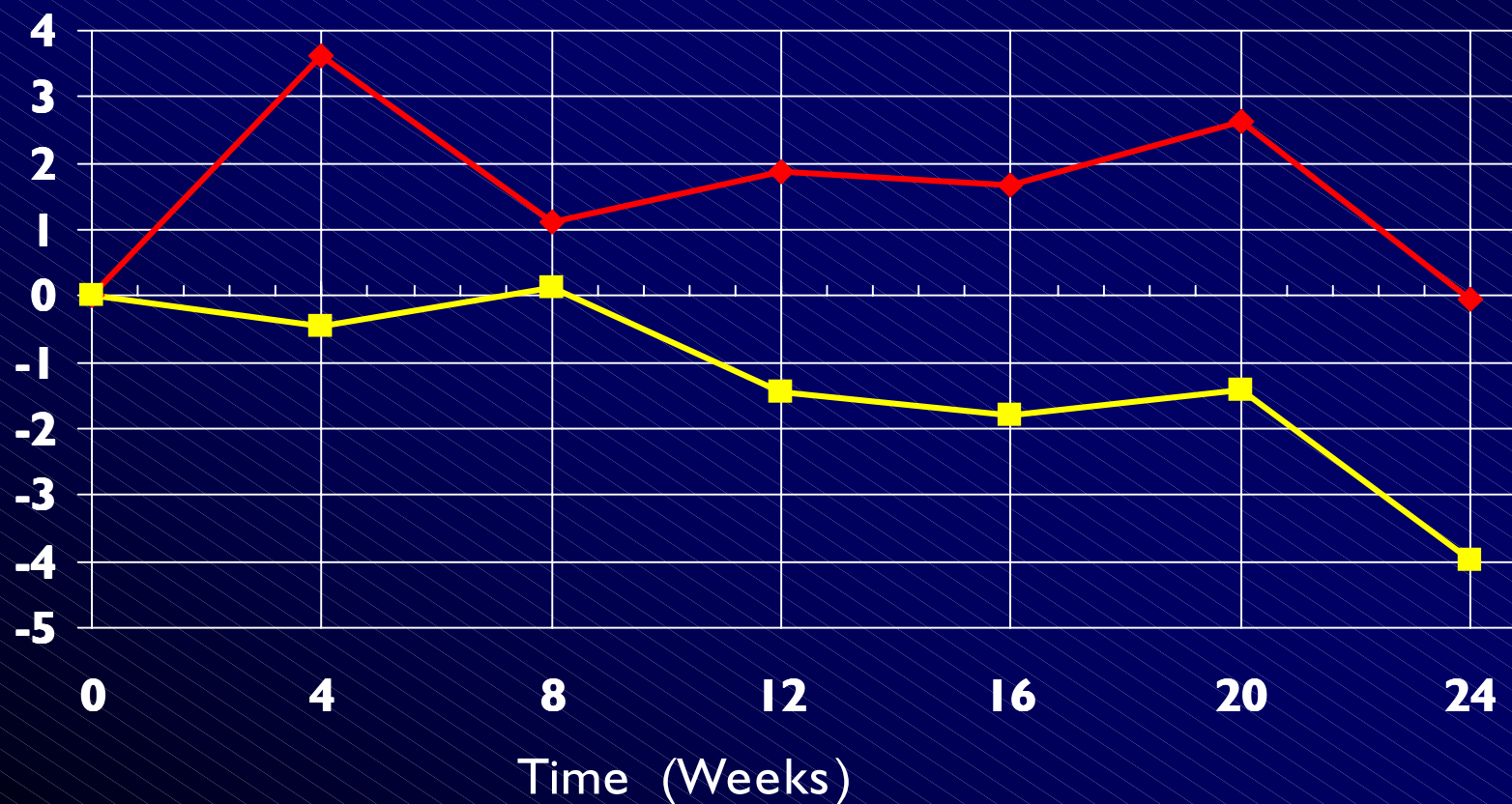
# Quality of Life Scales

Physical Function Index: Change in baseline by Drug



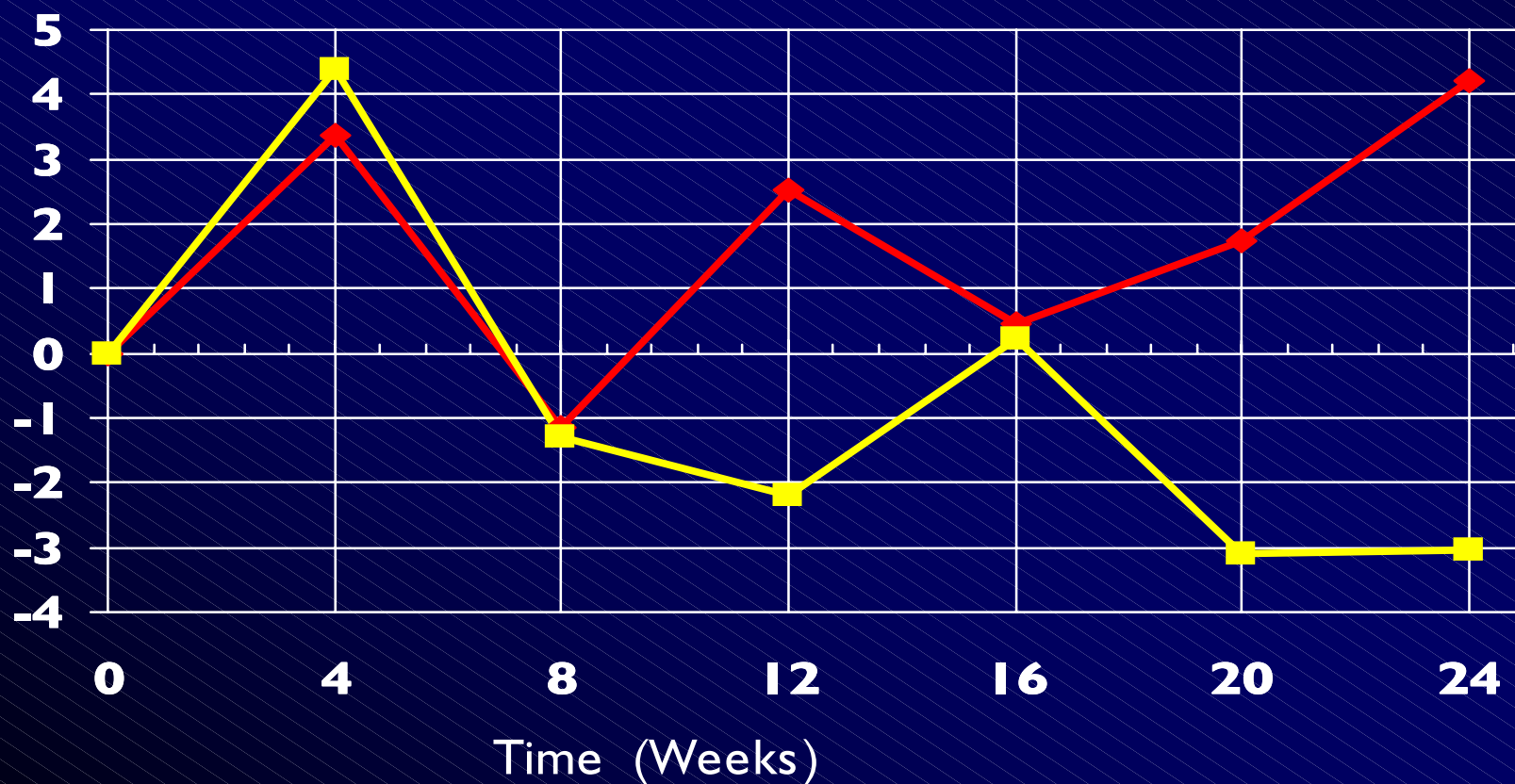
# Quality of Life Scales

Vitality: Change in baseline by Drug



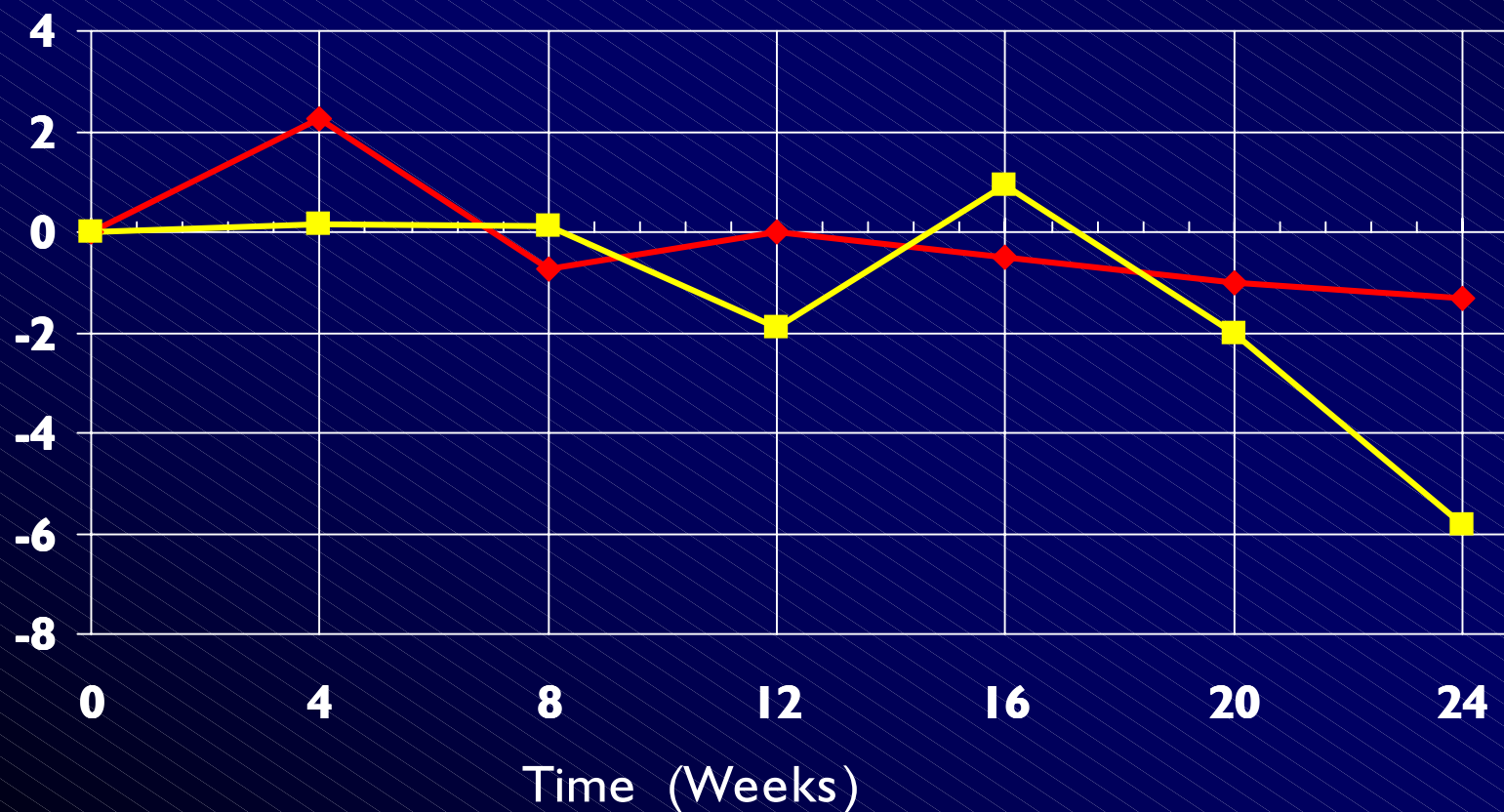
# Quality of Life Scales

Role Emotional: Change in baseline by Drug



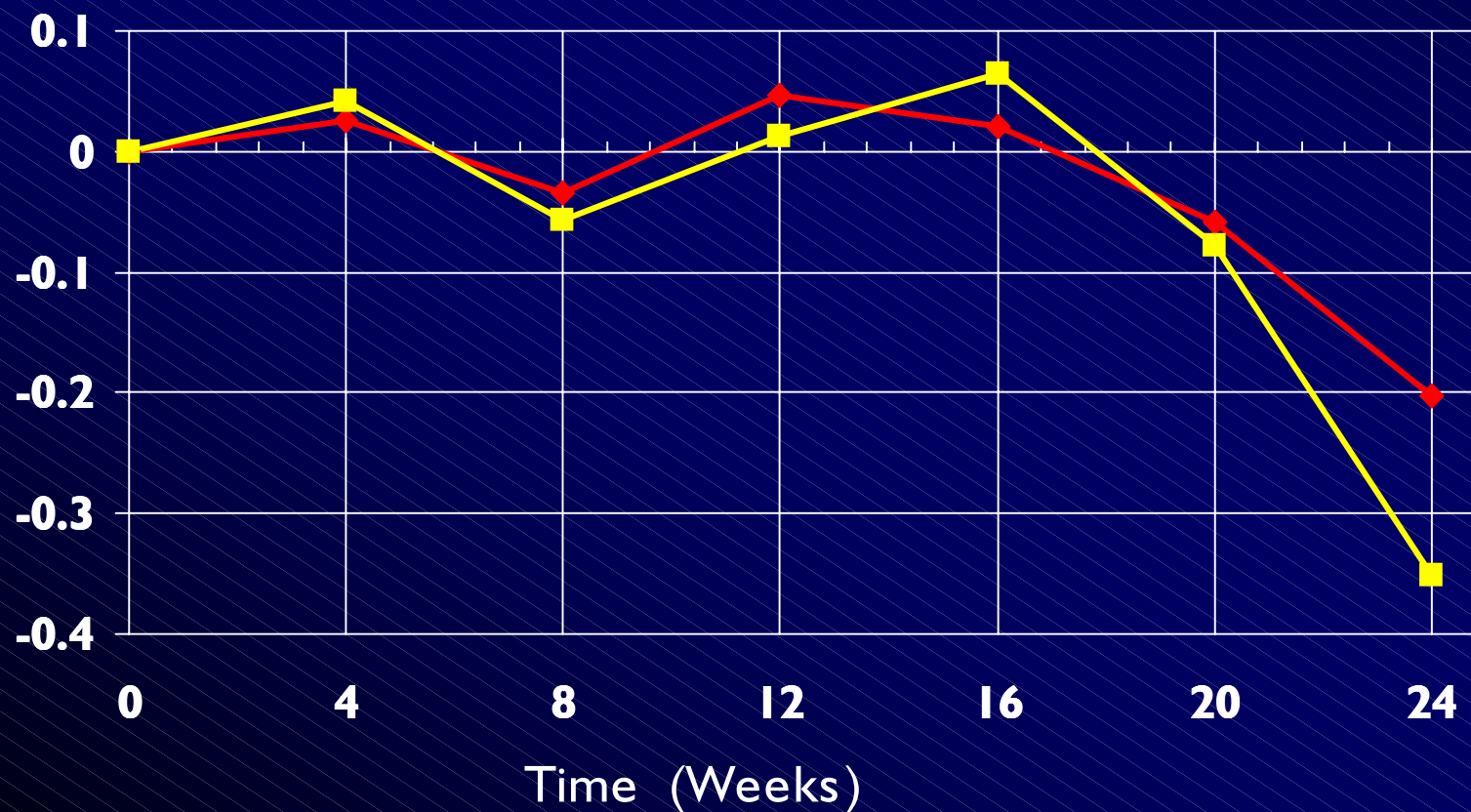
# Quality of Life Scales

Social Functioning: Change in baseline by Drug



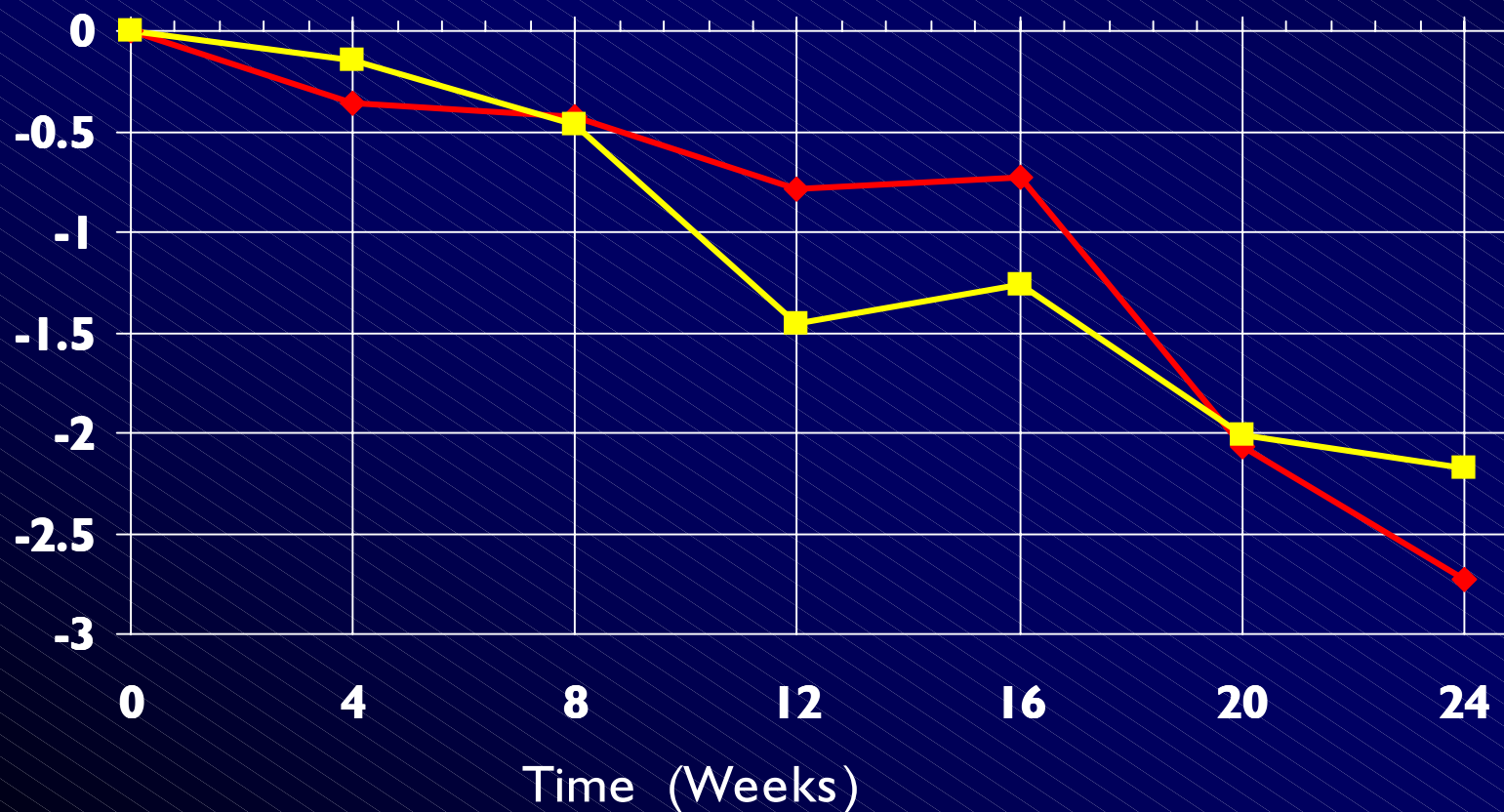
# Quality of Life Scales

Spitzer: Change in baseline by Drug



# Quality of Life Scales

Karnofsky: Change in baseline by Drug



# Clinical Study Results

## New Drug compared to Continued AZT

- CD4 counts were about 40 cells higher in the new drug group over the first 24 weeks of the study
- Other than study discontinuation for adverse reactions there were few clinical differences between the two study groups
- With 18 month follow-up there was a trend for a survival advantage and fewer hospitalizations for the new drug group



# Quality of Life

## Bio-Psycho-Social Model

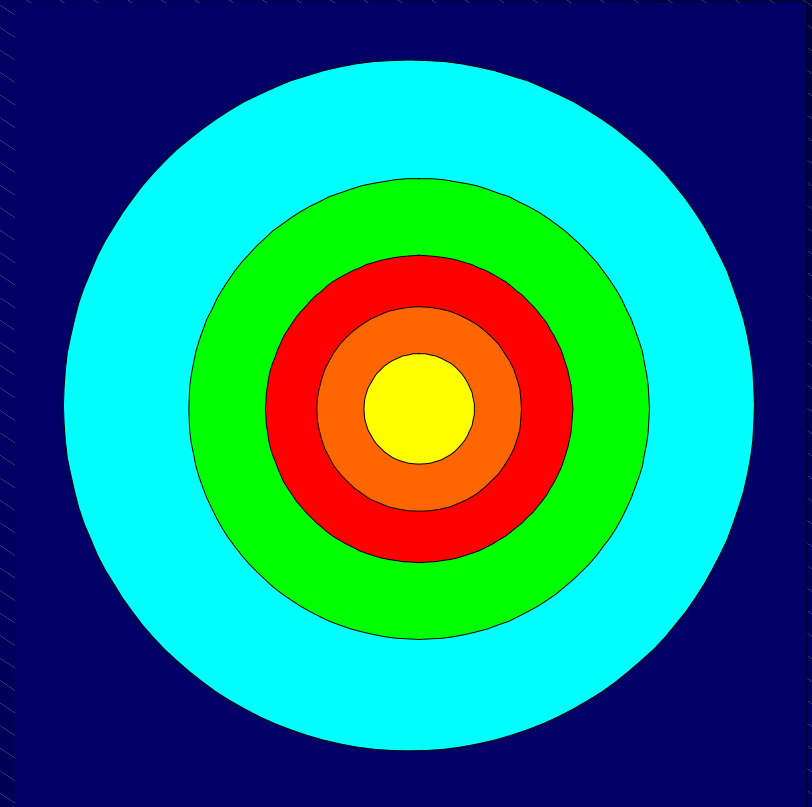
Organelle

Cell

Organ

Person

Family / Society



George Engle

# Quality of Life

## Bio-Psycho-Social Model

Organelle

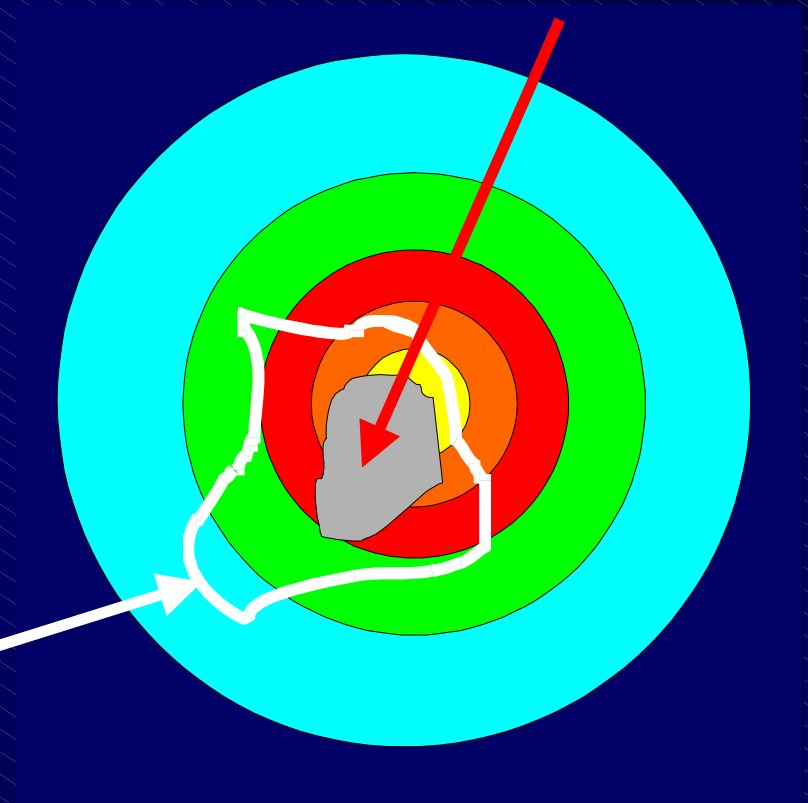
Cell

Organ

Person

Family / Society

Therapy Effect



Disease Effect

# Quality of Life

## Concerns

### ► Global Measures may be Less Sensitive

- e.g., a drug developed to relieve edema should have a larger impact on a congestive heart failure symptoms than on a QOL measure that edema effects indirectly
- e.g., adverse experiences will be better detected directly than through their effects on QOL

# Quality of Life

## Concerns

### ► Lack of Standardized Instruments

- Many clinical trials have "custom" instruments that might be tailored to favor the sponsor's treatment
- Lack of interpretability by clinicians and patients
- Lack of comparative experience across trials

# Quality of Life

## Concerns

- Potential to integrate risks and benefits

### Conceptual

- Is the integration meaningful to the patient ?
  - e.g., wearing corrective lenses and death on the same scale
  - e.g., considering social functioning and symptoms together rather than separately

# Quality of Life

## Concerns

### ► Potential to integrate risks and benefits

#### Temporal

- Adverse experiences mostly occur early  
Clinical benefits mostly occur late
- Methods may not adequately distinguish reversible from irreversible adverse experiences
- Results may be sensitive to duration of follow-up
- Study drop out after adverse experiences is common and creates analysis problems

# Quality of Life

## Advantages

- ▶ Focus on illness rather than disease
  - patient centered, not laboratory based
- ▶ Potential for standardized assessment method
- ▶ Potential to assess relative impact of events
  - Traditional clinical end-points may be mixtures of events
  - The events in the mixtures do not have the same impact
- ▶ Potential to integrate risks and benefits
  - Traditional approach considers efficacy and adverse experiences separately

# Quality of Life

## Proposed Uses\*

- A basis for choice between two agents with similar efficacy
- A tool to study compliance by learning the impact of treatment on QOL
- A method to quantify pain, distress and other subjective outcomes
- A measure of utility in cost-effectiveness studies



# Quality of Life

## Role in Therapeutic Development

- Primary endpoint ?
- Secondary measure to support primary finding ?
- Basis for comparative claim for equally effective drugs ?  
(which implies measuring adverse experiences)
- Advertising claim ?

Center for Devices and Radiological Health  
CDRH